Sanofi	XRP0038 (Riferminogene pecaplasmid, NV1FGF, temusi)
Mechanism of Action	Non-viral fibroblast growth factor 1 (NV1FGF) is a recombinant DNA plasmid in a pCOR backbone allowing expression of human FGF1
Overview	The purpose of this treatment is to provide therapeutic angiogenesis via intramuscular (IM) injection of a non viral gene vector, with the subsequent local release of FGF1 for the treatment of peripheral artery disease (PAD). Several nonclinical studies conducted in various animal models support the development of NV1FGF. IM administration of NV1FGF has been shown to express FGF1 protein in the injected muscle and to restore a functional vascular network in the ischemic limb in two animal models of hind-limb ischemia. pCOR plasmids are very narrow-host range plasmid vectors for non viral gene therapy. Such plasmids can only replicate in πprotein-producing enterobacteria, considerably limiting their host range. pCOR selection requires expression of a synthetic amber suppressor tRNA gene specific for phenylalanine. This can correct an *E. coli* argE amber mutation, making it possible for the recombinant host strain to grow on a minimal medium lacking arginine on which bacteria without the plasmid cannot grow. A specific *E. coli* host was constructed to support NV1FGF pCOR replication and selection.
Safety/Tolerability	The overall incidence of adverse events is high, especially for infections, worsening of peripheral ischemia, and cardiovascular events, similarly to the incidence observed in the placebo arm, and related to the underlying condition. Data do not indicate an increased incidence of retinopathy, cancer, or renal impairment in the NV1FGF-treated population. No immune response was observed in PAD patients following several doses or different regimens of NV1FGF. Pharmacokinetic investigations showed that in all dose regimens and at all dose levels, NV1FGF was rapidly cleared from the circulation (half-life in the plasma: 5-6 minutes). There was no evidence of accumulation in the circulation from repeated administration. Furthermore, there was no evidence of circulating FGF1 protein at any dose regimen or at any dose level, confirming the local nature of the NV1FGF IM treatment.
Additional Information	No clinical studies have been conducted in healthy subjects. In patients, 4 clinical studies were conducted in PAD patients with Critical Limb Ischemia (CLI) population with skin lesions (PM101, PM105, PM201/Talisman, and PM202), and one study was conducted in patients with intermittent claudication (IC) (PM211). A 50% reduction in the amputation rate was observed in the PM201 study (secondary endpoint). A Phase 3 study in patients with CLI with skin lesions (EFC6145) was performed. Phase 3 TAMARIS trial did not meet its primary endpoint, e. g., the superiority of NV1FGF vs. placebo in the prevention of major amputation or death.
Suitable for and Exclusions	
Clinical Trials	http://clinicaltrials.gov/ct2/results?term=XRP0038
Publications	http://www.ncbi.nlm.nih.gov/pubmed?term=NV1FGF